AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

1. (Currently Amended) A modified plasminogen activator inhibitor type-1 ("PAI-1") ~~PAI-1~~ molecule comprising a helix D region, an A3 strand, an A4 strand and an A5 strand, said molecule having an active form ~~which displays one or more functional activities of an active form of a wild-type PAI-1 protein~~, said molecule comprising ~~an~~ the amino acid sequence which has at least about ~~80%~~ 95% similarity to SEQ ID NO:2, in which two or more amino acid residues ~~that do not contain a sulfhydryl group in said corresponding wild-type PAI-1 protein~~ are each substituted by an amino acid residue that contains a sulfhydryl group, such that one or more disulfide bridges are formed between or within said helix D region, A3 strand, A4 strand and/or A5 strand of said modified PAI-1 molecule, and wherein said active form of said modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of ~~said active form of said~~ a corresponding wild-type PAI-1 protein.

2. (Original) The modified PAI-1 molecule of claim 1 which has an in vivo half-life of over 3 hours, 6 hours, 10 hours, 20 hours, 50 hours, 60 hours, 70 hours, 90 hours, 100 hours, 150 hours, 200 hours, 10 days, 12 days, 16 days, 30 days, or 60 days.

3. (Canceled)

4. (Original) The modified PAI-1 molecule of claim 1 wherein said residue that contains a sulfhydryl group is cysteine.

5. (Currently Amended) A modified plasminogen activator inhibitor type-1 ("PAI-1 ") ~~PAI-1~~ molecule having an active form in which two or more amino acid residues ~~that do not contain a sulfhydryl group in a corresponding wild-type PAI-1 protein having an active form~~ are each substituted by an amino acid residue that contains a sulfhydryl group, wherein: said active form of said modified PAI-1 molecule has an ~~in vivo~~ *in vivo* half-life that is longer than the ~~in vivo~~ *in vivo* half-life of ~~said active form of said~~ a corresponding wild-type PAI-1 protein; and

said two or more amino acid residues ~~that do not contain a sulfhydryl group~~ are selected from among positions 31, 97, 192, 197, 347, and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

6. (CurrentlyAmended) ~~The~~ A modified ~~PAI-1~~ plasminogen activator inhibitor type-1 ("PAI-1") molecule having an active form in which two or more amino acid residues ~~that do not contain a sulfhydryl group in a corresponding wild-type PAI-1 protein having an active form~~ are each substituted by an amino acid residue that contains a sulfhydryl group, wherein:
said active form of said modified PAI-1 molecule has an ~~in vivo~~ *in vivo* half-life that is longer than the ~~in vivo~~ *in vivo* half-life of ~~said active form of said~~ a corresponding wild-type PAI-1 protein; and
said two or more amino acid residues ~~that do not contain a sulfhydryl group~~ are selected from one or more pairs of amino acid positions including 31 and 97, 192 and 347, and 197 and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

7. (Original) The modified PAI-1 molecule of claim 1 that further comprises one or more amino acid substitutions that are not substitutions with a sulfhydryl-containing residue.

8. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule inhibits urokinase plasminogen activator.

9. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule inhibits tissue plasminogen activator.

10. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule augments endogenous PAI-1 function.

11. (Currently Amended) A method of producing a modified ~~PAI-1~~ plasminogen activator inhibitor type-1 molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule comprising a helix D region, an A3 strand, an A4 strand and an A5 strand, said modified PAI-1 molecule having an active form ~~which displays one or more functional activities of an~~

~~active form of a wild-type PAI-1 protein~~, said molecule comprising ~~an~~ the amino acid sequence which has at least about ~~80%~~ 95% similarity to SEQ ID NO:2, in which two or more amino acid residues ~~that do not contain a sulfhydryl group in said corresponding wild-type PAI-1 protein~~ are each substituted by an amino acid residue that contains a sulfhydryl group, such that one or more disulfide bridges are formed between or within said helix D region, A3 strand, A4 strand, or A5 strand of said modified PAI-1 molecule, and wherein said active form of said modified PAI-1 molecule has an ~~in vivo~~ *in vivo* half-life that is longer than the ~~in vivo~~ *in vivo* half-life of ~~said active form of said~~ a corresponding wild-type PAI-1 protein; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

12. (Currently Amended) A method of producing a modified ~~PAI-1~~ plasminogen activator inhibitor type-1 ("PAI-1") molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule having an active form ~~which displays one or more functional activities of an active form of a wild-type PAI-1 protein~~, said molecule comprising ~~an~~ the amino acid sequence which has at least about ~~80%~~ 95% similarity to SEQ ID NO:2 in which two or more amino acid residues ~~that do not contain a sulfhydryl group in said corresponding wild-type PAI-1 protein~~ are each substituted by an amino acid residue that contains a sulfhydryl group, wherein said active form of said modified PAI-1 molecule has an ~~in vivo~~ *in vivo* half life that is longer than the ~~in vivo~~ *in vivo* half-life of ~~the active form of said~~ a corresponding wild-type PAI-1 protein; and

(b) culturing the cell under conditions suitable for expression of the modified ~~PAI~~ PAI-1 molecule,

wherein said two or more amino acid residues ~~that do not contain a sulfhydryl group~~ are selected from among positions 31, 97, 192, 197, 347, and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

13. (Currently Amended) A method of producing a modified ~~PAI-1~~ plasminogen activated inhibitor type-1 ("PAI-1") molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule having an active form ~~which displays one or more functional activities of an active form of a wild-type PAI-1 protein~~, said molecule comprising ~~an~~ the amino acid sequence which has at

least about ~~80%~~ 95% similarity to SEQ ID NO:2 in which two or more amino acid residues ~~that do not contain a sulfhydryl group in said corresponding wild-type PAI-1 protein~~ are each substituted by an amino acid residue that contains a sulfhydryl group wherein said active form of said modified PAI-1 molecule has an ~~in vivo~~ *in vivo* half life that is longer than the ~~in vivo~~ *in vivo* half-life of ~~the active form of said~~ a corresponding wild-type PAI-1 protein; and (b) culturing the cell under conditions suitable for expression of the modified ~~PAI~~ PAI-1 molecule,

wherein said two or more amino acid residues ~~that do not contain a sulfhydryl group~~ are selected from one or more pairs of amino acid positions including 31 and 97, 192 and 347, and 197 and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

14. (Previously presented) A method of treating a disease or disorder related to aberrant angiogenesis in a subject in need thereof, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

15. (Withdrawn) A method of treating cancer in a subject suffering therefrom, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

16. (Withdrawn) The method of claim 15 wherein said cancer is selected from the group consisting of breast cancer, colon cancer, ovarian cancer, lung cancer, prostate cancer, melanoma, leukemia, lung cancer, skin cancer, pancreatic cancer, bladder cancer, sarcoma, and uterine cancer.

17. (Withdrawn) A method of treating a cardiovascular disease or disorder in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

18. (Withdrawn) The method of claim 17 wherein said disorder is hyperfibrinolysis, hemophilia, or vessel leakage syndrome.

19. (Withdrawn) A method of treating a disease or disorder that is mediated by uPA, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

20. (Withdrawn) A method of treating a disease or disorder that is mediated by tPA, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

21. (Withdrawn) A method of treating uPA-mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

22. (Withdrawn) A method of treating tPA mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

23. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the modified PAI-1 molecule of claim 1; and a pharmaceutically acceptable carrier.

24. (Previously Presented) The modified PAI-1 molecule of claim 1 wherein said A3 strand and A5 strand each comprises a top and a bottom part, said one or more disulfide bridges are formed linking said top part of A3 strand, said top part of A5 strand, said bottom part of A3 strand, said bottom part of A5 strand, and/or said helix D region.

25. (Canceled)

26. (Previously Presented) The modified PAI-1 molecule of cl aim 1 wherein each said substitution by an amino acid residue that contains a sulfhydryl group is at position 10-40, 70-120, 150-220, 300-342, 343-350, and 351-400 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

27. (Previously Presented) The modified PAI-1 molecule of claim 1 wherein said one or more disulfide bridges are formed at position 29-32, 92-107, 180-197, 246-249, 341-353, 353-374, and 381-391 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

28. (Previously Presented) The modified PAI-1 molecule of claim 1 wherein said one or more disulfide bridges are formed at positions 10-40 and 70-120; and/or 150-220 and 300-350 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering.

29. (Currently Amended) A modified PAI-1 molecule comprising an amino acid sequence of SEQ ID NO:2 ~~with substitutions at positions 31 and 97, 192 and 347, and/or 197 and 355, wherein at least 2, 4, or 6 amino acid residues at positions 31 and 97, 192 and 347 and/or 197 and 355~~ wherein amino acid residues at positions: (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347 and 355; or (vii) 31, 97, 192, 197, 347, and 355, are substituted with amino acid residues that contain a sulfhydryl group.

30. (Currently Amended) A method of producing a modified ~~PAI-1~~ plasminogen activator inhibitor type-1 ("PAI-1") molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule of claim 28; and
(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

31. (Currently Amended) A method of producing a modified ~~PAI-1~~ plasminogen activator inhibitor type-1 ("PAI-1") molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule of claim 29; and
(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.